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THE ACID-BASE STATUS OF HUMAN INFANTS IN RELATION TO BIRTH ASPHYXIA AND THE ONSET OF RESPIRATION

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Earlier studies[1] have led to the conclusion that respiratory failure in the newborn is due to anoxia. The aim of the present study has been to evaluate the birth status of the infant and to time the onset of respiration in relation not only to the arterial oxygen saturation but also to the carbon dioxide tension (Pco_2), the pH, and the total available buffer. Although the pH and pCO_2 have been measured previously,[2-5] they have not been considered as reflecting the duration of an episode of asphyxia. The term "asphyxia," as defined by Schmidt,[6] has been adopted since it denotes a simultaneous decrease both in the intake of oxygen and the elimination of carbon dioxide, i.e., anoxia plus hypercapnea. The way in which hypoventilation or asphyxia changes these variables, producing first a respiratory acidosis followed by a superimposed metabolic acidosis,[6-11] has been extensively reported in animals and adults.

MATERIAL AND METHODS

Blood samples were obtained from the artery and vein in a clamped segment of the umbilical cord at the moment of delivery. The samples were collected in greased syringes, the dead spaces of which were filled with a concentrated heparin solution.

Analysis of the samples for oxygen, carbon dioxide, oxygen capacity,[12] pH,[13] and hematocrit[14] was performed as soon after collection as possible, usually within 2 hours, the samples being rotated in iced water. The majority of oxygen saturations were measured by a manometric method.[12] Several bloods were analyzed with the double scale cuvette oximeter[15] or by the method of Nahas using the Beckman spectrophotometer.[16] All three methods were standardized against the manometric analysis of Van Slyke.[17] The microgas analysis was found to vary by ± 1 per cent[12] while

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the standard deviation of the differences was for the Beckman ± 1.3 per cent over the entire range, and for the cuvette oximeter ± 2 per cent over 40 per cent saturation and ± 3.5 per cent below 40 per cent.

The Pco_2 and buffer base (BB) were calculated from the Singer and Hastings nomogram[67] using the pH, the CO_2 content, and the hematocrit. The term "buffer base" refers to the total available buffer and includes both the bicarbonate (or alkali reserve), the protein, and the hemoglobin. In the study of metabolic acidosis, it is a more valuable measurement than the bicarbonate alone.

The recent work of Dawes and associates,[18] on the fetal circulation, indicates that the umbilical artery blood represents the blood going to the fetal tissues and not fetal venous blood. Contrary to earlier studies by Barcroft and his associates[19, 20] and Huggett,[21] the blood supplying the brain contains only slightly more oxygen than that in the umbilical artery (Fig. 1).[22] The more accurate interrelationship of the oxygen saturations in the various vessels was obtained by withdrawing blood from eight major vessels simultaneously rather than using discrete samples collected over a period of time. Since the cineangiographic evidence of Lind and Wegelius[23] suggests that the fetal circulation in the human being resembles that in the lamb, the umbilical artery has been taken to represent the blood supplying the tissues of the infant at the moment of delivery.

One minute after the complete birth of the infant, he was evaluated and given a score.[24] Two points were given for each of the following: color, respiration, muscular tone, nasal irritability, and heart rate. All the infants with a score of 8, 9, or 10 are vigorous and have breathed within seconds of delivery. In this group, scores less than 10 have reflected a lower score for color. The infants with a score of 4 or less are blue and limp and have failed to establish respiration by one minute. With increasing depression the last two vital signs, reflex irritability and heart beat, disappear, in that order.

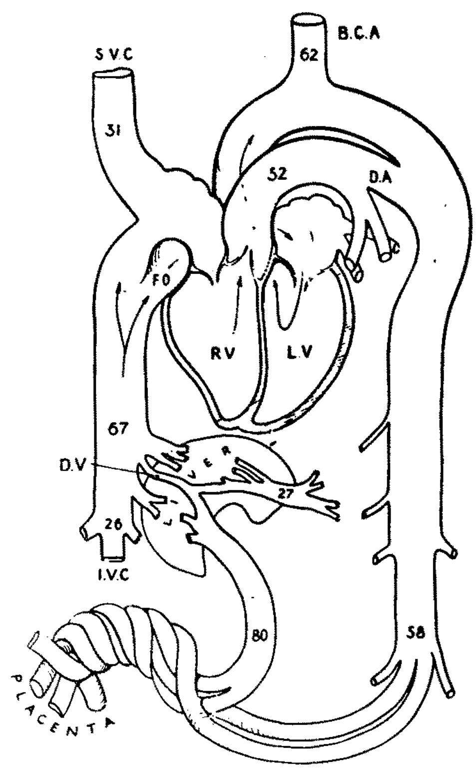

Fig. 1.—Diagram of the fetal circulation. The figures indicate the percentage oxygen saturation of blood withdrawn simultaneously from various vessels, and averaged from determinations on 6 lambs. **I.V.C., inferior** vena cava; S.V.C., superior vena cava; D.V., ductus venosus; F.O., foramen ovale; D.A., ductus arteriosus; B.C.A., brachiocephalic artery. (*From* Changes in the Heart and Lungs at Birth, Cold Spring Harbor Symposia on Quantitative Biology, Vol. XIX, 1954.)

The time required for the infant to establish spontaneous and continuous respirations is termed, "time to sustained respiration." (T.S.R.)

To determine the biochemical status of the depressed group, samples from either the umbilical artery, the portal vein area in the liver, or from the right or left atria have been used. This has been considered justifiable for several reasons. In many of these infants the heart rate is slow and the pulse feeble. The blood pressure has not yet been measured at this time, but from the response of infants 2 to 11 days old[25] and from that of newborn and fetal lambs[26] to severe anoxia, it is likely to be low. Therefore, the cord circulation will be poor, especially if there is compression. Frequently, the cord is collapsed and bloodless or the blood is present in loculated sections between areas of complete occlusion. In such cases, a sample of the circulating blood from the infant, either arterial or venous, if obtained before the onset of respiration, will give a more reliable indication of his condition. All the portal vein samples were obtained during resuscitation (artificial expansion of the lungs under positive pressure) about the time the first spontaneous breath was taken. Consequently, the oxygen level will be higher, the P_{CO_2} somewhat lower, and the pH higher than prior to the resuscitation. However, the BB, which returns to normal relatively slowly, may be expected to indicate more accurately the severity of the asphyxia.

RESULTS

The biochemical analyses of the umbilical cord blood of 101 babies are presented in Table I and Figs. 2 and 3. The data have been arranged according to the type of delivery (vaginal or section) and the Apgar score of the infant at one minute.

There is a wide range in the oxygen levels in both the umbilical artery and vein blood and in the A-V difference. All the infants exhibited some degree of asphyxia with a low oxygen saturation and a high CO_2 tension. Of the 63 umbilical artery samples, 26 had an oxygen saturation below 10 per cent and 7 had no measurable oxygen. Fourteen of these severely anoxic infants were not depressed (score 8 and 9) and cried spontaneously within seconds of delivery (Fig. 2). Four were in the intermediate group (score 5 to 7) and 8 were in the depressed group (score 0 to 4). The highest umbilical artery oxygen saturation recorded was 51 per cent.

The umbilical artery pH ranged from 7.00 to 7.35, with a mean of 7.26 for the vigorous and 7.14 for the depressed infants. The P_{CO_2} ranged from 39 to 98 mm. Hg, with a mean of 55 for the vigorous and 74 for the depressed infants, indicating a respiratory acidosis.

A depression of the BB below the normal of 42 mEq./L. for pregnant women (normal for adult males 47 to 50) revealed the presence of a superimposed metabolic acidosis in a number of instances (Fig. 3).

A comparison has been made between the pH, and P_{CO_2}, and BB in either portal vein or umbilical artery blood in the depressed infant and umbilical artery samples from the vigorous group (Table II). Both the pH and BB are significantly lower while the P_{CO_2} is significantly higher in the depressed infants. $p < .01$. The severe degrees of metabolic acidosis

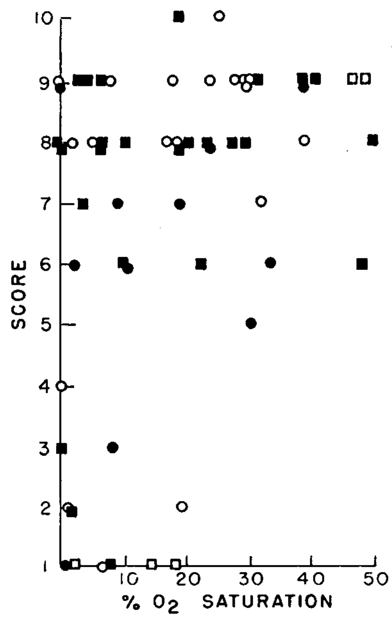

Fig. 2.

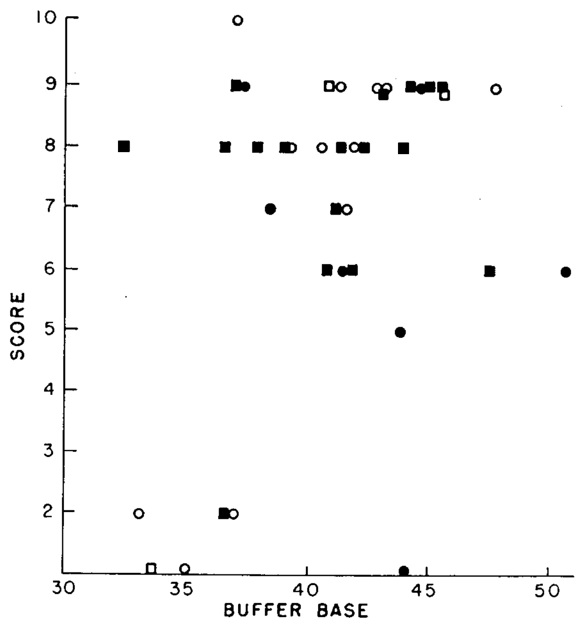

Fig. 3.

Figs. 2 and 3.—○ Vaginal delivery—regional anesthesia; ● Vaginal delivery—inhalation anesthesia; ■ Cesarean section—regional anesthesia; □ Cesarean section—inhalation anesthesia.

Fig. 2.—Umbilical artery—oxygen saturation. Comparison of clinical status of infant at birth with arterial oxygenation.

Fig. 3.—Umbilical artery—buffer base. Comparison of clinical status of infants at birth with arterial buffer base.

TABLE I. BIOCHEMICAL FINDINGS IN THE UMBILICAL ARTERY AND VEIN

NO.	NAME	SCORE	OXYGEN % SAT.		pH		P_{CO_2} MM. HG		BB MEQ./L.		ANESTHESIA AND COMPLICATIONS
			ARTERY	VEIN	A	V	A	V	A	V	
		8-10		*Regional Anesthesia*				*Vaginal Delivery*			
1	Lo	9	0	24	7.32	7.42	45	39	41	46	None
2	Mo	8	2	29	7.19	7.27	62	50	39	41	Spinal
3	Bur	8	6	68	–	7.20	–	45	–	37	None
4	Vel	8	7	67	–	–	–	–	–	–	Caudal
5	Sc	9	9	–	7.26	–	59	–	43	–	Pudendal
6	Irv	9	–	30	–	–	–	–	–	–	Saddle
7	Thos	10	–	45	–	7.24	–	39	–	42	Pudendal
8	Pier	8	17	59	7.20	7.28	63	49	41	42	Pudendal
9	Bal	9	19	48	–	7.40	–	42	–	47	Spinal
10	Me	8	19	64	–	7.27	–	40	–	37	Epidural
11	Yo	9	25	34	–	–	–	–	–	–	None
12	Sant	9	28	–	7.31	–	48	–	43	–	Pudendal
13	Rod	9	30	–	7.37	–	47	–	48	–	Spinal
14	Jack	9	30	65	7.27	7.32	–	40	–	41	Pudendal
15	Jo	9	30	–	7.33	–	48	–	45	–	Caudal
16	Ha	10	31	61	7.15	7.20	64	49	37	37	Caudal
17	Wo	8	45	72	–	7.36	–	35	–	42	Caudal
Average			19.8	47.6	7.26	7.29	54.5	42.8	42.1	41.2	
								Cesarean Section			
18	Jo	8	0	72	–	–	–	–	–	–	Spinal
19	Do	8	0	23	–	–	–	–	–	–	Spinal
20	Hi	9	3	15	–	–	–	–	–	–	Spinal
21	Ro	9	5	12	7.30	7.41	50	36	43	45	Spinal
22	Ca	9	6	9	–	7.17	–	69	–	39	Spinal
23	Sch	9	7	29	7.10	7.22	64	46	37	38	Spinal
24	Lev	8	7	10	–	–	–	–	–	–	Spinal
25	Tr	8	11	23	7.10	7.12	77	69	36	36	Spinal
26	Mi	10	19	72	–	–	–	–	–	–	Spinal
27	Rod	8	19	30	7.14	7.19	81	70	38	39	Spinal
28	Sh	8	–	13	–	7.24	–	63	–	43	Spinal
29	Fo	9	–	40	–	7.26	–	50	–	41	Spinal
30	Ri	8	–	41	–	7.20	–	57	–	39	Spinal
31	Ha	10	–	72	–	7.20	–	51	–	39	Spinal
32	Mag	8	21	44	7.22	7.29	54	43	39	40	Spinal
33	Lo	8	24	53	7.27	7.31	53	41	42	41	Spinal
34	Sc	9	–	31	–	–	–	–	–	–	Spinal
35	Bur	8	28	67	7.27	7.29	50	43	41	41	Spinal
36	Ri	8	30	32	7.04	7.17	74	51	32	35	Spinal
37	Pr	9	32	65	7.33	7.35	51	44	45	45	Spinal
38	Reu	9	32	51	7.26	7.29	59	51	44	43	Spinal
39	Men	9	39	70	7.30	7.36	54	45	45	45	Spinal
40	Ra	9	41	62	–	–	–	–	–	–	Spinal
41	O'R	8	51	79	7.33	7.37	45	37	44	45	Spinal
Average			19.7	42.3	7.22	7.26	59.3	50.9	40.5	40.8	
				Inhalation Anesthesia				*Vaginal Delivery*			
42	Rei	9	0	34	7.33	7.37	59	45	37	39	Cyclopropane
43	Rad	8	25	67	7.26	7.33	–	–	–	–	Cyclopropane
44	Da	9	39	65	–	7.28	–	47	–	41	Cyclopropane
45	Go	8	–	–	7.25	7.25	49	47	42	41	Cyclopropane
46	Li	8	–	44	–	–	–	–	–	–	Cyclopropane
47	New	8	–	47	–	–	–	–	–	–	Cyclopropane
48	Deigh	10	–	62	–	7.31	–	46	–	–	Cyclopropane
49	May	8	–	63	–	7.30	–	46	–	–	Cyclopropane
50	Kr	8	–	68	–	–	–	–	–	–	Cyclopropane
51	Ga	9	–	69	–	7.46	–	–	–	–	Cyclopropane
52	Meu	8	–	68	–	–	–	–	–	–	Cyclopropane
53	Ro	9	–	75	–	7.33	–	49	–	–	Cyclopropane
54	Mo	9	–	79	–	7.46	–	32	–	47	Cyclopropane
Average			21.3	61.7	7.28	7.35	54	44.5	39.5	42.0	

TABLE I—CONT'D

NO.	NAME	SCORE	OXYGEN % SAT. ARTERY	OXYGEN % SAT. VEIN	pH A	pH V	P_{CO_2} MM. HG A	P_{CO_2} MM. HG V	BB MEQ./L. A	BB MEQ./L. V	ANESTHESIA AND COMPLICATIONS
								Cesarean Section			
55	Ch	9	48	78	7.27	7.31	49	42	41	42	Cyclopropane
56	Ru	9	49	85	7.30	7.35	52	48	45	46	Cyclopropane
Average			48.3	81.5	7.28	7.33	50.5	44.9	43.2	43.9	
				Inhalation Anesthesia				*Vaginal Delivery*			
57	To	8	9	29	7.28	7.33	46	40	41	42	N_2O
58	Br	8	–	26	–	–	–	–	–	–	N_2O
59	Ha	8	18	30	7.20	7.26	–	–	–	–	N_2O
60	Va	9	–	45	–	7.33	–	50	–	46	N_2O
61	Camp	8	23	–	7.33	–	51	–	47	–	N_2O
62	Men	9	44	–	7.40	–	39	–	46	–	N_2O
63	Pier	8	–	81	–	7.29	–	–	–	47	N_2O
Average			23.5	42.2	7.30	7.30	45.3	45	44.6	45.0	
		5-7		*Regional Anesthesia*				*Vaginal Delivery*			
64	Dur	6	–	35	–	7.25	–	55	–	42	Pudendal
65	Mil	7	33	56	7.36	7.45	39	32	42	44	Caudal
66	DeJ	6	–	57	–	7.28	–	48	–	–	Caudal
67	Ray	5	–	61	–	7.37	–	43	–	–	Caudal
Average			33	52.2	7.36	7.33	39	44.5	42	43	
								Cesarean Section			
68	Beau	7	4	31	7.21	7.33	67	45	41	43	Spinal
69	Aiel	6	10	32	7.22	7.33	64	43	42	42	Spinal
70	Beas	6	23	30	7.16	7.23	69	57	41	41	Spinal
71	Ortiz	6	48	84	7.39	7.39	44	40	47	47	Spinal
72	Ja	5	–	83	–	–	–	–	–	–	Sample before delivery
Average			21.2	52.0	7.24	7.32	61.0	46.2	42.7	43.2	
				Inhalation Anesthesia				*Vaginal Delivery*			
73	Gai	6	2	40	7.21	7.24	69	55	42	41	Cyclopropane
74	Mel	7	9	42	7.23	7.22	53	46	38	37	Cyclopropane
75	Gib	6	11	48	7.22	7.29	92	54	51	46	Cyclopropane
76	Val	7	19	37	7.25	7.28	–	–	–	–	Cyclopropane
77	Riv	5	30	47	7.23	7.26	67	56	44	44	Cyclopropane
78	Rei	7	–	49	–	–	–	–	–	–	Cyclopropane
79	Ley	7	–	54	–	7.36	–	39	–	43	Cyclopropane
80	Len	5	–	72	–	–	–	–	–	–	Cyclopropane
81	Kel	6	34	73	7.27	7.32	–	–	–	–	Cyclopropane
Average			17.5	51.3	7.23	7.28	70.2	50.0	43.7	42.2	
				Inhalation Anesthesia				*Cesarean Section*			
82	Pi	5	4	11	–	7.35	–	38	–	40	Cyclopropane
								Vaginal Delivery			
83	Pa	7	14	24	7.23	7.23	56	54	43	43	N_2O
		0-4		*Regional Anesthesia*				*Vaginal Delivery*			
84	Gou	4	0	17	–	–	–	–	–	–	Caudal
85	Sua	2	1	9	7.01	7.03	99	93	33	34	Saddle
86	Bu	1	7	–	7.08	–	78	–	35	–	Caudal
87	Wa	1	–	21	–	7.28	–	57	–	43	Pudendal
88	Fried	2	19	34	7.18	7.25	57	46	37	39	4+ nucal cord with facial petechiae; spinal
Average			6.7	20.2	7.09	7.18	78.0	65.3	35.0	38.6	
								Cesarean Section			
89	Per	3	0	10	–	–	–	–	–	–	Spinal
90	Em	2	1	41	7.17	7.20	63	53	38	38	Cord prolapse thru wound for 2 min.
91	Mer	1	7	63	–	–	–	–	–	–	Local and Pentothal
Average			2.6	38.0	7.17	7.20	63	53	38	38	

TABLE 1—CONT'D

NO.	NAME	SCORE	OXYGEN % SAT. ARTERY	OXYGEN % SAT. VEIN	pH A	pH V	P_{CO_2} MM. HG A	P_{CO_2} MM. HG V	BB MEQ./L. A	BB MEQ./L. V	ANESTHESIA AND COMPLICATIONS
					Inhalation Anesthesia			*Vaginal Delivery*			
92	Ga	1	0	0	7.08	7.07	94	93	34	34	Cyclopropane
93	Ha	1	–	21	–	–	–	–	–	–	Cyclopropane
94	Br	3	15	51	–	7.27	–	61	–	46	Cyclopropane
95	Su	1	18	38	7.00	7.11	–	–	–	–	Ruptured uterus; Cyclopropane
Average			11.0	27.5	7.04	7.15	94	77.5	34	40	
								Cesarean Section			
96	Mul	1	0	62	7.32	7.37	53	40	44	44	{Cyclopropane 4+ nucal cord
97	Fent	3	8	27	7.32	7.38	–	–	–	–	Cyclopropane
98	Pier	2	–	29	–	7.33	–	44	–	43	Cyclopropane
Average			4	39.3	7.32	7.36	53	42	44	43.5	
								Vaginal Delivery			
99	Wa	1	–	42	–	7.07	–	71	–	33	Ether
100	Tr	1	–	67	–	7.25	–	49	–	41	Prolapsed cord; ether
101	Mer	3	–	56	–	7.26	–	50	–	41	Chloroform
Average				55		7.19		56.6		38.3	

and derangement of pH and P_{CO_2} which were observed as a result of prolonged apnea are illustrated in Table III and Fig. 4. Here the portal vein or atrial samples taken at the onset of respiration have been compared with the biochemical status of the cord blood when samples could be obtained. In all instances, the biochemical measurements in the portal vein blood showed a greater degree of asphyxia.

DISCUSSION

These studies have revealed the varying degrees of asphyxia which occur during all forms of delivery. Contrary to earlier reports,[1, 4, 5] an infant may make the initial respiratory gasps with no measurable oxygen in his arterial blood. In this sense, anoxia, as measured by the oxygen saturation of the umbilical artery's blood, correlates poorly with postnatal vigor. The significant difference which has been demonstrated between the vigorous and depressed infants lies in the pH, P_{CO_2}, and BB (Table II). Previous studies have shown that these variables give a measure of an asphyxial insult,[6-11] a brief period of asphyxia causing in the main a respiratory acidosis with a raised P_{CO^2} and little change in the BB. This pattern of change may be seen in the vigorous infants (score 8-10, Table I). If on the other hand, the asphyxia is prolonged, a marked reduction in the BB occurs (depressed infants score 0-4, Table I), indicating a metabolic acidosis which has become superimposed on the respiratory acidosis.

From this it is evident that the response of the infant to asphyxia is identical to that of the adult.[6-11] The rapid recovery after birth[29] also follows the adult pattern. In the vigorous infants the absence of a severe metabolic acidosis in the presence of a high P_{CO_2} indicates that the period of asphyxia has been quite brief. In

Table II. Statistical Comparison of Vigorous and Depressed Infants

	Vigorous infants (score 8-10) umbilical artery samples			Depressed infants (score 0-4) umbilical artery or portal vein			
	Number	Mean	S.D.	Number	Mean	S.D.	p
O_2	43	22.2	21.77	12	6.3	7.3	
pH	30	7.26	0.085	10	7.04	0.142	$p < .01$
PCO_2	27	55.3	10.25	9	82.0	19.93	$p < .01$
BB	27	41.5	3.68	10	31.4	6.93	$p < .01$

Table III. Babies Severely Depressed at Birth

			Changes in pH, Pco_2, and BB with time				
Name	Score	Site	Oxygen % saturation	pH	Pco_2	BB	
Fr	2	Umbilical artery	19.2	7.18	57.0	37.0	Spinal anesthesia, cord tightly round neck; facial petechiae; T.S.R.,* 3 min., 35 sec.
		Portal vein	21.2	6.98	90.2	30.5	P.V. sample 25 sec. after first spontaneous respiration
Fe	3 ↓	Umbilical artery	8.0	7.32			Anesthesia cyclopropane; thick meconium-stained mucus in pharynx
at 3 min.	1	Portal vein	50.9	7.10	77.0	37.8	T.S.R., 12 min.; P.V. sample 2 min. after first spontaneous respiration
Wa A Twins	1	Umbilical vein	41.9	7.06	70.5	33.2	Anesthesia chloroform; twins locked, 2 weeks premature; T.S.R., 25 min.
A		Portal vein	61.9	6.91	69.5	24.1	P.V. sample 2 min. after first spontaneous respiration
B	1	Portal vein	55.9	6.80	114.5	21.7	P.V. sample 1 min. after first spontaneous respiration
Ch	0	Left atrium	93.0	6.74	39.9	$<$15.0	Emergency section for prolapsed cord; no heartbeat at birth, cardiac massage Sample after 25 min. of artificial ventilation when infant took first spontaneous gasp

*T.S.R. = time from birth to spontaneous respiration.

light of this, earlier interpretations that the fetus is normally adjusted to these high tensions of carbon dioxide[27] can no longer be accepted.

The high score group of infants, those who were well oxygenated, had little or no depresion of the BB. Where the oxygen saturation was 10 per cent or less in this group, in all but one case the BB value was slightly below the average for the group but well above the average for the depressed infants. The low BB values occasionally seen in this group were associated in most instances with a second stage of labor of 2 hours or more or slowing and irregularity of the fetal heart during the first stage of labor. This undoubtedly reflects anoxia during labor which is sufficient to disturb metabolism but not enough to depress the infant significantly.

Several factors probably contribute to the asphyxia which appears to occur as a normal phenomenon in almost every delivery.

Cord Compression.—

Any reduction in the blood flow through the cord will lower the arterial oxygenation since the fetal venous blood (26 to 31 per cent saturated in the lamb[22]) will be passing directly into the arterial circulation with little or no mixing with oxygenated blood from the placenta. The saturation in uration between the umbilical artery blood and that in the vein, which may be found in this last situation. Manipulation of the cord causes constriction of the umbilical arteries, which in turn slows the stream of blood through the placenta. Barcroft[30] has vividly described the acute sensitivity of these vessels, particularly at term.

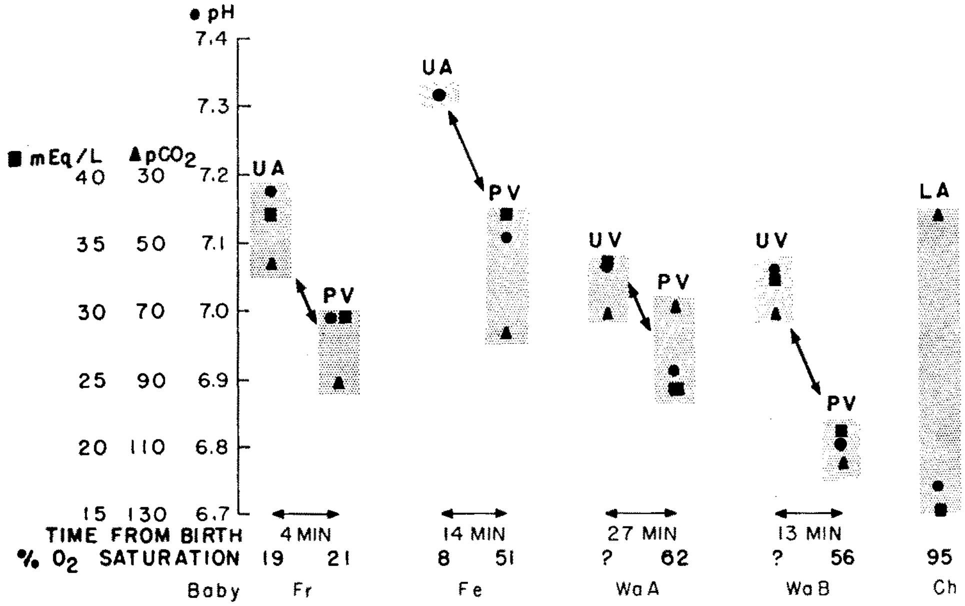

Fig. 4.—Changes in pH, pCO_2, and buffer base in 5 depressed newborn infants. UA—umbilical artery; UV—umbilical vein; PV—portal vein; LA—left atrium. The same umbilical vein sample has been used for comparison in twins Wa A and Wa B.

The values for Ch represent pure metabolic acidosis remaining after 25 minutes of resuscitation. The oxygen saturation in the LA was 99 per cent.

the umbilical vein will remain unchanged[30] or may even be raised, since the fetal blood will remain in contact with the blood in the intervillous space for a longer period; but with reduction in flow, this blood does not reach the fetal circulation. The reduction in flow can be caused by kinking, prolapse, pressure between the fetus and the rim of the pelvis or vagina, or when the cord is wound tightly round the neck. Clemetson and Churchman[31] have shown the large difference in sat-

Changes in Uterine Blood Flow.—

a. *Posture:* The supine position has been shown to be associated with compresion of the mother's inferior vena cava by the heavy gravid uterus. Howard and his associates[32] have demonstrated that the pressure in the femoral vein may be raised from 108 to 239 mm. H_2O by this mechanism. This rise will decrease the pressure gradient between the uterine artery and vein and will tend to reduce blood flow through the uterus. When the obstruction to the inferior vena cava is more complete, sufficient to cause hypotension in the mother,[33] an even greater reduction in flow will occur. This factor must be considered in cesarean section during which the mother may be flat on her back for 15 or 20 minutes before the baby is delivered. It is probable that the occasional very low oxygen value obtained in both cord vessels at cesarean section under local anesthesia is caused partly by this obstruction effect[34] (Table I).

b. *Hypotension with spinal anesthesia or maternal hemorrhage:* Hypotension not infrequently produced by spinal anesthesia will reduce the pressure gradient and the uterine flow. Fetal distress revealed by excessive movements or slowing of the fetal heart occurs under such conditions. Whether because of hypotension, increased uterine tonus, or some other factor as yet undetermined, the oxygen saturation in lambs delivered under spinal anesthesia is uniformly lower than in those delivered under pentobarbital.[35] Henderson reports a similar finding in human beings in comparing spinal and inhalation anesthesia.[36] Hypotension as a result of hemorrhage is likely to have an even more profound effect on reducing the uterine flow.

c. *Uterine contraction:* Caldeyro-Barcia[37] has shown that with a strong uterine contraction, blood flow through the uterus and placenta is completely arrested.

Uterine vein samples withdrawn a short time before delivery of the fetus by cesarean section[38] show, in most instances, a higher oxygen saturation than does umbilical vein blood obtained after delivery from a clamped segment of cord. This is contrary to the figures which Barron and Meschia[39] give in studies on the placental exchange of respiratory gases in the sheep and rabbit, and suggest that in the few minutes between the sampling from the uterine vein and delivery of the infant a reduction in oxygen transfer has occurred. Changes in the uterine circulation with manipulation, incision, and the immediate contraction which occurs as the amniotic fluid gushes out could account for this difference.

d. *Partial separation of the placenta:*

This will reduce the effective area of diffusion and will lead to a lower oxygenation of the fetus.

Reduction in the Maternal Exchange of Respiratory Gases.—

a. *Breath holding and straining:* Both of these occur during vaginal delivery, when anesthesia is not given or is minimal, and may result in a significant lowering of the maternal arterial oxygen saturation.

b. *Inhalation anesthesia:* The effect of inhalation anesthesia upon fetal oxygenation varies as much with the agent being used as with the clinic reporting the study. Good and poor results have been claimed for all agents. Because of a variety of techniques and the many additional factors noted above, it is difficult to determine the effect of the agent itself. However, if the mother has any airway obstruction during anesthesia, her CO_2 elimination and oxygen uptake will be impaired. This effect will be reflected in the fetus if delivery is prolonged.

It has been assumed by some authors that samples obtained at cesarean section under regional anesthesia represent normal in utero conditions in the human being.[28] This has led to the concept of "Everest in utero" and to the belief that, with placental aging, fetal arterial oxygen saturation falls as term approaches.[40, 41] However, any sample obtained either at vaginal delivery or cesarean section is unlikely to represent the normal conditions before labor or operation since both uterine blood flow and cord compression cannot be controlled. The multiple factors enumerated above, acting separately or in combination, will all tend to lower the oxygenation of the fetus at delivery. While cord compression will increase the difference in saturation between the umbilical artery and vein, all the other factors will tend to lower the oxygenation of both vessels since they interfere with the exchange between mother and fetus. Undoubtedly, this accounts for the low average but the very wide range in published figures (10 to 60 per cent saturation in the umbilical artery and 10 to 84 per cent saturation in the umbilical vein[3-5, 28, 31, 34, 40-47] [Table IV]). The highest human figures reported are almost identical with the normal value which Dawes and associates[35] and Barron and Meschia[39] observed for lambs. These high values, rather than the average, probably give a truer indication of the normal in utero environment. Further indirect evidence which supports a high intrauterine oxygen environment is found in the color photographs of the unborn human infant taken by means of hysterophotography.[48] Here the infant actually appears to be pink.

An interesting advance has been the development of techniques for sampling intervillous blood in human beings during labor.[49] Prystowsky[49] has observed a low oxygen tension in the intervillous space and a marked reduction in the maternal-fetal oxygen tension gradient when the infant proved to be in poor condition at birth. The maternal samples were taken just prior to delivery. While the range of oxygen tension in the intervillous sample was wide in the normal group (72 to 26 mm. Hg), in all but three instances, the individual tensions were considerably below a value which would be compatible with an umbilical vein oxygen saturation of 80 per cent. Such findings indicate that, when the head is on the perineum prior to delivery, the various maternal factors tending to lower the fetal oxygenation may already be in action.

Table III and Fig. 4, showing the differences between the cord blood

TABLE IV. COMPARISON OF OXYGEN SATURATION IN UMBILICAL CORD VESSELS

AUTHOR	AVERAGE PER CENT OXYGEN SATURATION		NUMBER OF CASES		RANGE		DELIVERY
	ARTERY	VEIN	ARTERY	VEIN	ARTERY	VEIN	
Eastman[28]	16	50	15	15	6-27	38-58	Vaginal vertex
	30	63	1	1			Caesarean section
Smith[42]	16	51	37	40	2-48	16-81	
Clemetson & Churchman[31]	31	63	10	12	2-50	35-84	Vaginal vertex Spontaneous vaginal vertex
Walker[41]	20	48	9	10	1-28	13-60	Spontaneous vaginal vertex
Rooth & Sjostedt[34]	32	61	69	98	0-62	9-83	Spontaneous vaginal vertex
Present authors (See Table I)	22	49	43	55	0-51	9-85	Cesarean section and vaginal vertex; all vigorous at birth

samples and those obtained from the portal vein, indicate that anoxia causes rapid changes in the pH, P_{CO_2}, and BB. The speed of change as recorded here may be misleading since there was severe cord compression in one infant and one umbilical vein sample has been compared to the two portal vein samples in the case of the twins. However, the rapidity of these changes is well documented in studies on both dogs[8, 9] and adult man.[50] Where the residual air in the lungs has not been washed out with oxygen, the saturation falls to zero in 3 minutes (dogs) and to 28 per cent in 2 minutes (adult man).

The results of the present study emphasize the need for obtaining a sample from within the depressed infant if the limits of respiratory and metabolic acidosis are to be revealed. It is quite possible that these levels may be dangerous enough to cause irreversible cellular damage in the newborn human. If they occur as rapidly as this study suggests and are dangerous, the need for the greatest dispatch in resuscitating an infant with no oxygen reserves is apparent.

Asphyxia in Relation to the Onset of Respiration.—

In vitro and in vivo studies demonstrate that the brain is depressed by oxygen lack,[51, 52] even slight lowering of the oxygen tension depressing the respiratory center.[53] However, through the action of the chemoreceptors which are stimulated by anoxia and continue to function when the oxygen tension has fallen to zero,[6] this depression may be almost completely masked. Under severe anoxia, breathing takes the form of gasps in which the accessory muscles play a major role. The first gasps of the newborn infant are of this type but are soon replaced by quiet and relatively regular diaphragmatic and intercostal breathing following the rapid expansion of the lungs and oxygenation which normally occur within minutes of delivery.[54-56] Although Miller and Behrle[57] have suggested that the chemoreceptor response is poor in the first 24 hours of life, the occurrence of vigorous first breaths under extreme anoxia provides indirect evidence that the chemoreceptors are indeed functioning actively at birth. It is possible that they may be functioning at a higher threshold which was not reached during the induced hypoxia studies of Miller. The direct recording of action potentials from the proximally severed sinus nerve in newborn and fetal animals by Cross and Malcolm[58] is further evidence of activity.

As in the adult, the respiratory center of the infant is acutely sensitive to carbon dioxide[59, 60] and is probably stimulated both directly[61] and indirectly[6] when the P_{CO_2} rises. The high P_{CO_2} shown in most vigorous newborns is likely to play a major role in the first gasp if the anoxia is not severe. Finally the low pH, acting through the chemoreceptors,[6] and the flood of sensory impulses crowding in from the skin, the muscles and the joints[62] doubtless constitute important stimuli of the first breaths. These will be augmented by stimuli from the rapidly adapting stretch receptors in the alveoli[63] as the lungs expand.

With progressively severe asphyxia, a point is reached when the respiratory center is finally so depressed that it is unable to respond.[51] The P_{CO_2} and pH which previously stimulated the cells now act as depressants. Schmidt has termed this the Reversal. The exact levels of P_{CO_2} or pH which will depress the center appear to vary depending on the oxygen level, the degree of metabolic acidosis, and the presence or absence of narcotic drugs.[63-65] As for adults, the multiple factor theory of Gray[66] is the most acceptable to interpret the response of the infant respiratory center. All four factors must be considered in each individual case.

Although the infant may take his first breath when there is no measurable oxygen in umbilical artery blood, the presence of oxygen appears to be essential if respiration is to occur in the presence of severe respiratory and metabolic acidosis. This is apparent not only in the vigorous infants (Table I) who have a particularly high P_{CO_2} or low BB but also in the depressed group. In the latter, spontaneous respiration occurred only after artificial oxygenation of the infant.

When anesthetic or narcotic agents are present in significant amounts, spontaneous respiration is seen only when the asphyxia is mild (Cyclopropane cases, score 8-10, Table 1). With high dosage, when drugs are almost wholly responsible for the apnea, the infant frequently makes his first gasp after an interval of 1 to 2 minutes probably as a result of the stimuli arising as the asphyxia increases (infants receiving cyclopropane, score 5-7). These are the infants who appear vigorous, with good tone and heart rate, yet fail to breathe immediately. In other instances in which asphyxia is already severe, a small dose of anesthetic or narcotic will appear to cause profound depression.

SUMMARY AND CONCLUSIONS

1. Some degree of asphyxia, usually of brief duration, occurs as a result of the delivery process and is a normal finding in all births. This may be caused by several factors operating on the fetal and maternal circulations at the time of delivery. Because of these factors, the cord blood obtained following delivery of the infant can rarely, if ever, give a true indication of the normal intrauterine environment.

2. The blood in the umbilical artery represents the blood supplying the fetal tissues, the blood which reaches the head and upper extremities containing on the average only 4 per cent more oxygen. The blood in the umbilical vein will be related more to the placental exchange at or just prior to delivery and may bear little relation to the fetal arterial oxygen level.

3. Vigorous respiration can occur spontaneously in the absence of measurable oxygen in the umbilical artery blood.

4. Asphyxia produces the same biochemical changes in the infant as in the adult—a respiratory acidosis followed by a superimposed metabolic acidosis.

5. The effects of asphyxia, if not too prolonged, acting through the chemoreceptors, are probably responsible for the initial gasps of the infant.

6. Failure to breathe at birth is caused by either depressant drugs or the severity of the respiratory and metabolic acidosis, the result of prolonged asphyxia.

7. The pH, P_{CO_2}, and BB of the newborn infant's blood give a measure of the degree of an anoxic insult. They may change rapidly if he fails to breathe.

8. In evaluating the biochemical status of a depressed infant, a blood sample taken directly from the infant is more representative of his status than is a sample from the umbilical artery.

9. The severe degrees of metabolic and respiratory acidosis seen in depressed infants stress the need for active ventilation and re-oxygenation of these infants immediately after birth.

10. Since inhalation anesthesia administered to the mother will always augment the metabolic depression, regional anesthesia would seem more desirable for delivery of an infant with fetal distress.

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